In the Specification

Please amend the paragraph beginning at line 20 of page 23 as follows:

Figure 1A. Stereo view of the overlay of engrailed HTH region ($\alpha 2$-$\alpha 3$; 1ENH) and one EF-Hand of parvalbumin (5PAL), to illustrate that the helical axes are colinear. The C-terminal $\alpha 3$ is the homeodomain DNA-recognition helix. ~~Engrailed is shown in green, parvalbumin in blue, and the Ca(H) ion with its ligands in magenta.~~

Please amend the paragraph beginning at line 18 of page 45 as follows:

Chimeric Design and Synthesis. The 33-residue peptides shown in Figure ~~2B~~ 2 were based on overlays of engrailed and calmodulin crystal structures (Figure 1B). Known protein crystal structures were oriented manually using the freeware program SwissPDBViewer (Guex et al., 1997) to align the fold of the homeodomain HTH motifs and Ca-binding protein EF-Hand motifs. Crystal coordinates were downloaded from the Protein Data Bank (PDB) for several EF-Hand proteins, such as calmodulin (1OSA) (Chattopadhyaya et al., 1992), parvalbumin (5PAL) (Roquet et al., 1992), and calcineurin (1TCO) (Kissinger et al., 1995). Coordinates for the homeodomain proteins engrailed (with and without co-crystallized DNA, 2HDD and 1ENH, respectively) (Clarke et al., 1994; Kissinger et al., 1990; Tucker-Kellogg et al., 1997) and antennapedia with DNA (9ANT) (Fraenkel et al., 1998) were obtained. The best fits (determined by inspection and RMS deviation of small helical sections) were used.

Please amend the paragraph beginning at line 22 of page 50 as follows:

In order to maintain the same 3D orientation of $\alpha 2$ and $\alpha 3$, the last turn of $\alpha 2$ needed to be omitted when including the EF-loop. If just the four residues of the turn from the HTH were replaced, then $\alpha 2$ was displaced in space one turn (about 4Å) in the N-terminal direction, destroying potential $\alpha 2$-$\alpha 3$ hydrophobic stabilization at the turn. Based on these observations, a peptide was designed and synthesized (Figure 2). P3 comprises $\alpha 2$ and $\alpha 3$ of engrailed (T_{27} -L_{34} and E_{42}-K_{57}) and the twelve-residue consensus EF-Hand Ca-binding loop (Falke et al., 1994). Three additional residue substitutions were made ($X_{(n)}$ denotes numbering scheme). The substitution of $A_{43} \rightarrow R_{(19)}$, the residue which occurs in the related Antennapedia homeodomain sequence, incorporated an additional basic residue to strengthen electrostatic interactions with

DNA. A second modification ($Q_{44} \rightarrow E_{(20)}$) maintained the conserved Glu at the twelfth position of the EF-Hand loop, and the $W_{48} \rightarrow H_{(24)}$ substitution was incorporated for ease of synthesis by Fmoc chemistry. Based on the parent crystal structures, sites of Ca(II) or Ln(III) binding are indicated by an x~~, sites of phosphate backbone contact with an o, and DNA base contacts with a * for representative~~ P3.

Please amend the paragraph beginning at line 1 of page 56 as follows:

Moreover, as shown in Figure 8, EuP3 catalyzes the cleavage of supercoiled, double-stranded DNA as well as model compounds. The conversion of supercoiled plasmid (type I) to open circular (type II), linear (type III), or smaller fragments was monitored by agarose gel electrophoresis. Because the synthetic peptides bind strongly to DNA, thus preventing the observation of products, the peptides were chelated prior to electrophoresis (Falke et al., 1994). At the point each reaction was quenched (0.1 M EDTA), a suspension of neutral, washed, cation resin (Amberlyst, 10-20 μL) was incubated with each sample for 30 minutes, spun down, and the supernatant loaded into wells. After 24 hours of reaction (incubated at 37° C), the concentration-dependent formation of open circular plasmid was observed (Figure 8). Higher concentrations of EuP3 are less effective (slower), in keeping with the model BNPP system. Also of note is that 25 μM EuP3 in the presence of 225 μM excess metal ~~(lane 3) has~~ <u>had</u> a similar effect to 25 μM EuP3 alone, suggesting that peptide bound to DNA blocks indiscriminate Eu cleavage. Over a 10-300 μM EuP3 gradient, nicking occurred from 10-150 μM, with the greatest amount of cleavage at 30 μM EuP3. EuP3 activity falls off with increasing concentration likely due to dimerization. Surprisingly, EuP4a activity does not.